

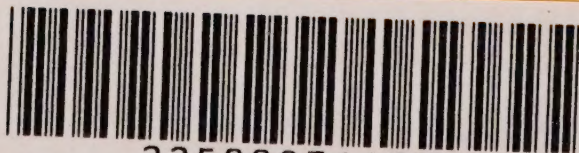
'ESCHATIN'

A Standardized Extract
of the Adrenal Cortex



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To the Medical Profession

‘ESCHATIN’

A Standardized Extract of the Adrenal Cortex

‘ESCHATIN’ is a highly purified, natural extract of the adrenal cortex containing not less than 50 dog-units of adrenal cortical activity per cubic centimetre.

The whole extract of the adrenal cortex has been separated into crystalline and amorphous fractions.

In his review of the subject of adrenal physiology, Stoffer (1945) states that it is evident that there is no fraction having all the functions of the adrenal cortex.

It is of considerable interest that the amorphous residue remaining after all the crystalline fractions have been removed is exceedingly potent. Kendall (1942) points out that “if each of the fractions of the whole extract is assayed by the method in which adrenalectomized dogs are maintained in a normal condition and the minimal amount which is required is determined, then the ‘amorphous fraction’ if properly prepared, can be shown to

possess by far the greatest activity."

Thus, there are many hormones in the adrenal cortex which exert different actions, and are chemically distinct. 'Eschatin', the whole extract of adrenal cortex, contains all these fractions in as nearly a natural state as it is possible to obtain them.

'Eschatin' is indicated in the treatment of Addison's disease, chronic cortical insufficiency without characteristic changes in pigmentation, pituitary myxœdema, and acute adrenal cortical insufficiency precipitated by surgical removal of adrenal tissue or associated with the Waterhouse-Friderichsen syndrome.

'Eschatin' is also of value in overcoming the symptoms of cortical insufficiency associated with shock due to trauma or burns. Severe infections, febrile diseases, hypotension, hypoglycæmia, asthenia, and toxæmia of pregnancy are also included among the less specific indications for 'Eschatin'.

ADMINISTRATION AND DOSAGE

'Eschatin' is administered by deep subcutaneous, intramuscular or in-

travenous injection ; the last method is recommended for emergencies only. The maximum effect following a single dose of 'Eschatin' is obtained within four to six hours. It is preferable, therefore, to administer the total daily dosage in equally divided doses every six to eight hours. Correspondingly larger doses are required if the total daily dose is given in one injection.

The dosage varies widely, depending on the degrees of cortical deficiency. In Addison's disease, an initial dosage of 1 to 5 c.c. daily, in divided doses, is suggested. In a severe crisis, however, 20 to 30 c.c. daily may be required.

In Addisonian crises sodium chloride may be administered by intravenous injection or by proctoclysis. When there is no emergency, adequate sodium chloride may be given in a high salt-diet together with 5 to 15 gm. of salt daily. Sodium Chloride 'Emplets' (enteric-coated tablets) each of which contains 1 gm. ($15\frac{1}{2}$ grs.) will be found particularly suitable for the purpose. If supplementary sodium chloride is given, 10 to 20 c.c. of 'Eschatin' daily may be

adequate. Smaller amounts are usually sufficient for maintenance after severe adrenal insufficiency has been controlled.

When used to relieve adrenal cortical deficiency symptoms in such conditions as asthenia or hypotonia, 1 to 3 c.c. weekly is suggested.

Children may be given 1 c.c. initially and the dose varied as indicated.

CLINICAL APPLICATIONS

It is now generally recognized that the adrenal cortex plays an important rôle in regulating the distribution of sodium, chloride, potassium, and water. It also plays an important part in carbohydrate metabolism and in pigment distribution. These, as well as other physiological activities of the adrenal cortex not yet clearly established, are functionally exhibited by active cortical extracts and probably account for the specific usefulness of 'Eschatin' in adrenal insufficiency.

As early as 1933, Swingle, *et al.*, called attention to the similarity of the symptoms of adrenal insufficiency and shock. Since that time a number of investigators have de-

scribed adrenal cortical changes associated with various infectious diseases such as diphtheria, scarlet fever, and acute peritonitis. Acute collapse with bilateral hæmorrhage into the adrenals is a clinical syndrome encountered in severe septicæmia. In an epidemic of meningococcal infections, Thomas (1943) noted that hæmorrhages into the adrenals had occurred in 17 of 23 fatal cases in which autopsies were performed. In patients suffering from post-operative shock, Weil and Browne (1939) observed a maximum excretion of cortin in the urine between the third and fifth days, thus demonstrating the increased output of adrenal cortical hormones in this condition.

In order to establish a correlation between morphological changes in the adrenal cortex and various systemic diseases, Sarasen (1943) examined the adrenal glands of 110 patients at autopsy.

Cortical enlargement associated with depletion of lipoid or reversal of lipoid pattern was found associated with inflammatory diseases, cachexia, pemphigus and protracted

emesis. Various neoplasms as well as extensive burns are known to be associated with adrenal enlargement and depletion of lipoid. Sarasen emphasizes that these conditions are associated with signs and symptoms of adrenal insufficiency of varying degree, and that death may be attributed to adrenal insufficiency.

ADRENAL CRISIS

Adrenal crisis may occur in patients with Addison's disease or chronic adrenal insufficiency as the result of intercurrent infections, in patients with "pituitary myxœdema" following thyroid therapy, in fulminating meningococcal meningitis, or following surgery involving the adrenal glands.

In such instances, drastic measures must be taken quickly. Treatment should include measures to maintain plasma volume and blood-pressure and intravenous administration of adequate amounts of 'Eschatin'. Infusion of physiological sodium chloride solution and 5 to 10 per cent glucose solution is suggested. (Thorn, 1944).

ADDISON'S DISEASE AND CHRONIC ADRENAL INSUFFICIENCY

According to Greenblatt (1945), adrenal cortex extract is of the utmost value in the treatment of Addison's disease. A diagnosis of Addison's disease is suggested if laboratory studies reveal hypoglycæmia, increased non-protein nitrogen and serum potassium and low serum chloride in the presence of clinical findings of gastro-intestinal disturbances, hypotension, marked asthenia, and progressive pigmentation.

Once diagnosis has been made, 'Eschatin' therapy should be instituted. The total daily maintenance dosage is preferably administered in divided doses at six to eight-hour intervals.

It is now generally recognized that there are many sub-clinical cases of adrenal insufficiency characterized by one or more symptoms such as anorexia, low blood-pressure, muscular weakness, hypoglycæmia and undue fatigability but without the pigmentation and other pronounced signs of Addison's disease. Some

of these conditions may be primary Addisonism, that is, constitutional dysfunction of the gland, and others may be secondary, that is, brought about by other causes such as infection and toxæmia. In many cases benefit may result from treatment with 'Eschatin' although there is often no means of proving adrenal insufficiency other than by the response to treatment.

ASTHENIA

The effect of adrenal cortex hormone in 32 cases of asthenia was studied by Gordon, *et al.* (1938). Fifteen of these cases were due to factors other than adrenal cortical insufficiency. The remaining 17 were promptly and definitely helped by administration of cortical hormone. Blood-pressure variations paralleled the clinical status of the patients and the intensity of therapy.

Discussing the treatment of tropical neurasthenia, Reed (1942) states that the first consideration in the treatment of this condition is the administration of cortical extract. This author recommends the use of 0.5 c.c. of adrenal cortical extract

('Eschatin') daily for ten consecutive days.

To overcome adrenal cortical deficiency in asthenia, treatment may begin with subcutaneous or intramuscular injection of 1 to 3 c.c. weekly. The dosage and number of treatments may be adjusted as conditions permit.

SHOCK

Severe pathological changes in adrenal cortex tissue frequently follow major surgical procedures, prolonged deep anæsthesia, extensive burns, or fulminating infections. Symptoms of adrenal insufficiency and the profound shock that may result from such changes can usually be overcome by adequate replacement therapy with 'Eschatin'.

In the treatment of burns, Wolff, *et al.* (1942), comment favourably on the use of adrenal cortical extract. These investigators state that the recovery period of third-degree burns was reduced to eighteen to twenty-four hours by the use of such extracts. The value of 'Eschatin' in the treatment of shock associated with burns has also been discussed

by Webb (1942), and by Rhodes, *et al.* (1941). It not only shortens the period during which protein leaks through the capillaries, but it also reduces loss of plasma, sodium, and chlorides, and assists in preventing increase in potassium.

When used to prevent surgical shock, it is suggested that 1 c.c. of 'Eschatin' be given one hour before operation, and 1 c.c. or 2 c.c. every six hours post-operatively until the patient is out of danger.

To overcome shock associated with extensive burns, larger doses are required.

FEBRILE AND INFECTIOUS DISEASES

Acute infections including meningococcal meningitis, puerperal sepsis, and lobar pneumonia may be associated with necrosis of adrenal cortex cells. (Rich, 1944). A possible relationship between adrenal cortical damage and circulatory collapse in such diseases suggests the use of 'Eschatin'. In a review of the clinical uses of adrenal cortical hormones, Lapin, *et al.* (1943), refer to a specific loss of the cortical fac-

tor in overwhelming infections as a possible cause of shock associated with such conditions.

Perla and Marmorston (1940) used cortical hormone as part of the treatment of severe infections including broncho-pneumonia, therapeutic malaria, and severe influenza. As a result of this plan of treatment circulatory collapse was avoided, there were decreased signs of toxicity, normal blood-pressure and appetite were maintained and the period of convalescence was shortened.

To combat the symptoms of adrenal exhaustion in infections it is suggested that 1 to 5 c.c. of 'Eschatin' be given daily with gradual reduction in dosage and frequency of injection as indicated.

TOXICOSES OF PREGNANCY

In publishing the results of adrenal cortex therapy in 78 cases of pregnancy toxæmia, Freeman, *et al.* (1937) stressed the efficacy and importance of this weapon in combating the vomiting of pregnancy. As used by the authors, this was a more reliable treatment than any they had tried previously.

Solomon (1941) states that the vomiting of early pregnancy can be controlled in many instances by giving small amounts of carbohydrate frequently, together with adequate sedation and that adrenal cortex and vitamin B₁ are definitely beneficial.

STANDARDIZATION

'Eschatin' is biologically standardized to contain not less than 50 dog-units of adrenal cortical activity per cubic centimetre. It contains less than 1 per cent of solid extractive material and is substantially free from the medullary hormone, adrenalin (less than 1 part in 1,000,000).

'Eschatin' is comparatively stable; if kept at refrigerator temperature its activity is maintained for more than a year. It should not, however, be subjected to heat sterilization. Because of the purity of 'Eschatin', untoward reactions following injections are rare.

PACKAGE

'Eschatin' is supplied in 10 c.c. rubber-capped vials.

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